REMARKS

Claims 1-29 are pending. Claims 1-9, 12-23, and 25-29 are rejected. Claims 10, 11, and 24 are objected to but the Examiner states would be allowable if rewritten in independent form to include the limitations of the base claim and any intervening claims. Claims 1 and 15 are presently amended. Claim 20 is canceled. As a result of this amendment and the discussion below, it is believed that all claims are patentable and that this application is now in condition for allowance.

Summary of the Invention of the Present Application:

The invention of the present application provides a composition and method for determining compliance with a medication regimen. This composition and method is rapid, simple, and inexpensive. In one embodiment, it includes an orally administrable composition in combination with at least one visual marker. This marker is present in a form and amount sufficient to cause a coloration of at least a portion of a mucous membrane or buccal membrane of the oral and/or pharyngeal cavity of a patient. In various embodiments of the invention, by way of non-invasive observation of this coloration of the mucous or buccal membrane of the oral and/or pharyngeal cavity, one may obtain information regarding patient compliance with a medication regimen, such as whether the medication has been taken, the time elapsed since the medication was last taken, whether it is time for another dose of medication, etc. Thus, the present invention is very rapid, simple, and non-invasive as opposed to more invasive, tedious,

and complicated monitoring methods of the prior art, such as the analysis of urine and stool samples, and injection of compositions.

Claim Rejections 35 U.S.C. § 102:

The Examiner has rejected claims 15-20, 22, and 29 under 35 U.S.C. § 102(b) as being anticipated by Singh (U.S. Patent No. 5,458,879). In particular, regarding claim 15, the Examiner states that Singh discloses an oral composition containing a coloring agent or marker wherein the composition coats and adheres to the throat and mucous membranes, and that visible coloration of the mucous membranes is an inherent property of the coloring agent. Applicants respectfully disagree.

Applicants note that Singh is directed to an aqueous oral composition including a mucoadhesive. The mucoadhesive is used to retain a medicament, such as an antitussive, in the throat for longer periods in order to enhance its effectiveness. Applicants further note that while Singh does mention colorants as an optional ingredient (including FD&C Red No. 40) in an oral composition, such colorants find their use solely for the purpose of imparting a particular color to the composition of Singh. They have no purpose and indeed teach no purpose beyond that. In other words, the colorants are used to provide an aesthetic, cosmetic characteristic (color) to the composition, much like a flavoring agent would be used to make the composition more palatable. In fact, at column 7, lines 45-46, Singh states that the purpose of the colorants is to produce a "pleasant looking final product." There is no teaching in Singh

that such colorants function as anything but as a superficial component for aesthetic and cosmetic purposes. That is, they are essentially optional components with respect to the therapeutic action provided by the composition. The Singh reference does not inherently disclose utilizing a marker in a form and sufficient amount to cause coloration of a patient cavity enabling subsequent visual observation to determine compliance with a medication regimen. Further, claim 15 has been presently amended to recite that the half-life of the marker is comparable to the half-life of the composition. Support for this amendment may be found at least in originally filed claim 20. Applicants submit that the half-life of the colorant in Singh (based on the amounts disclosed) would not be similar to, and thus comparable to, the half-life of the composition. This, again, is because the colorant of Singh is only present in a small amount to be used as a optional component.

Applicants submit that the use of colorants as optional components in Singh is very apparent when one considers the disclosure of column 7, lines 42-47. The paragraph includes a mere list of ingredients which may be included in the composition. These ingredients may include "natural or artificial sweeteners, flavoring agents, colorants and the like." The subsequent Examples go on to simply list "colorants," including "FD&C Red # 40." However, there is no indication that the colorant plays any significant role in the composition of Singh, nor does Singh teach that the colorant is present in a form and amount sufficient to stain the oral and/or

pharyngeal cavity for subsequent visual observation to determine compliance with a medication regimen. In contrast, the marker of the composition of the present application is what allows an observer to determine compliance, duration since last medication, remaining time until next medication, etc. There simply is no teaching in Singh by which one of skill in the art may use the composition disclosed therein to obtain such information.

Further, as mentioned above, Applicants assert that there is absolutely no teaching in Singh that the colorant is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. First, Applicants submit that the composition of Singh is taught as having a wholly different purpose than that of the present application. Reference to the entirety of Singh makes it quite clear that the purpose of the composition of that reference lies in that it includes a mucoadhesive to promote retention of a medicament, such as an antitussive, in the oral and/or pharyngeal cavity. Nowhere does Singh discuss or teach that the colorant actually marks the adhesive and can be seen. Rather, as described above, the colorant of Singh is merely used to impart an aesthetic, cosmetic quality to the composition prior to injection. Second, Applicants submit that the amount of colorant in the Singh composition, while providing color to the composition, does not provide an amount sufficient to cause significant

coloration such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to be visually observable, as is required by claim 15. In support of this assertion, Applicants direct the Examiner's attention to the attached Affidavit of Gilbert R. Gonzales under 37 C.F.R. § 1.132.

In view of the above, Applicants respectfully request a withdrawal of the rejection of claims 15-20, 22, and 29 under 35 U.S.C. § 102(b).

The Examiner has rejected claims 15-20 and 29 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,303,102 (the Schlichte '102 patent). In particular, regarding claim 15, the Examiner states that the Schlichte '102 patent discloses a marker in combination with one or more treatment drugs, medicaments, or a composition applied topically or orally, wherein the marker is a pigment or dye providing visual evidence for gauging the application and time since the application of the medicine. Applicants respectfully disagree with the rejection.

Applicants submit herewith an affidavit under 37 C.F.R. § 1.131 stating that the composition claimed in the present application was conceived and reduced to practice in the United States prior to September 7, 2000, the filing date of the Schlichte '102 patent. Even though Applicants have submitted an affidavit to remove the

Schlichte '102 patent as a reference, for the reasons discussed below, Applicants also submit that the Schlichte '102 patent does not anticipate claims 15-20 and 29 of the present application.

Regarding the Schlichte '102 patent, Applicants first note that the entire patent is directed only to use in coloration of, and observation in, cutaneous or subcutaneous tissues. (See at least the title, "Cutaneously Applied..."; column 2, lines 19-20, "What is lacking...is a cutaneously applied ... composition"; column 2, lines 33-34, "The instant invention provides a ... composition which is applied cutaneously or subcutaneously"; column 5, lines 16-19, "the pigment vehicle carries a colored pigment or dye suitable for administration into the dermis, or subcutaneous tissue, e.g. the fatty layer underlying the dermis"; and column 14, line 28, "applied cutaneously.") In contrast, Applicants submit that independent claim 15 of the present application recites the marker as causing contact coloration of a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants further submit that the mucous and buccal membranes of the oral and/or pharyngeal cavity cannot be classified as cutaneous or subcutaneous tissues. The cutaneous and subcutaneous tissues make up the tissues of and relating to the skin. The mucous and buccal membranes recited in the claims of the present application, on the other hand, are mucous-secreting membranes that line the oral and/or pharyngeal cavity. These membranes and tissues are wholly different substances.

The Schlichte '102 reference teaches marking of such cutaneous or subcutaneous tissue primarily through injection, such as into the cutaneous or subcutaneous tissue. For example, the reference teaches that an inoculation could mark the underside of a hide, the hide itself (cutaneous) or the fat at the injection site. Another alternative is an implant(subcutaneous). A process involving injection of a marker (or implantation of a marker) is completely different from the contact coloration described in the present application and recited in the claims. Injection is invasive. Injection requires the passage of some amount of time for the marker to appear. These are some of the very drawbacks that are discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes. A system involving injection or implantation is not suitable for a medication regimen as described in the present application due to the drawbacks described above and discussed in the present application.

By contrast, the invention of the present application overcomes all the drawbacks associated with injection and implantation (and with markers designed to appear in cutaneous or subcutaneous tissues, as described in Schlichte), by providing and claiming an orally ingestable composition that colors the mucous or buccal membrane of the oral or pharyngeal cavity upon contact therewith. Such a method is simple and noninvasive. In contrast, nowhere is there a teaching or even a hint in the Schlichte '102 reference regarding a marker which is active for coloring a portion of a

mucous membrane or buccal membrane of the oral/pharyngeal cavity. In fact, nowhere in the Schlichte '102 reference do the words "membrane" or "membranes" even appear.

However, in the Office Action dated September 12, 2003 and in the recent Advisory Action dated November 21, 2003, the Examiner has stated and maintained that the Schlichte reference discloses a marker in combination with a composition which may be applied orally, wherein the marker provides visual evidence of application and time elapsed since application. In response, Applicants first note that the Examiner does not state that the Schlichte marker colors a membrane of the oral and/or pharyngeal cavity, as is recited in claim 15 of the present application. Applicants presume this may be because nowhere does Schlichte state this. Applicants do note, however, that discussion of an "oral" application of the marker formulation in Schlichte, or application of the formulation in the "mouth," appears at only three locations in Schlichte. First, in column 1, lines 7-9, Schlichte states that "[t]he present invention relates to a marker... applied either topically or orally." Second, in column 3, lines 22-23, Schlichte states that the "marker color will appear... in the mouth." And finally, in column 3, lines 28-30, Schlichte states that the marker formulation can "be injected or given orally at a given day and appear at a later date or appear in a few hours." Applicants submit that none of these statements teach the oral administration and contact coloration of membranes as disclosed and claimed in the present application.

Applicants submit that even though Schlichte mentions "oral" and "mouth," there is no suggestion that such application leads to coloration and subsequent observation of mucous membranes of the oral and/or pharyngeal cavity. Nor is such coloration necessarily inherent, since Applicants submit that a marker formulation may be ingested and subsequently appear at a site distant to the oral and/or pharyngeal cavity. Also, such a marker formulation could appear in tissues of the mouth, as opposed to membranes. In fact, Applicants assert that a reading of the instances of "oral" and "mouth" in Schlichte clearly shows that Schlichte does not contemplate a coloration of the mucous or buccal membranes of the oral or pharyngeal cavities.

For example, while oral application is mentioned in a perfunctory manner in the "Field of the Invention" section of Schlichte, that oral application is described in slightly more detail in column 3 of the "Detailed Description." Applicants submit that a person of ordinary skill in the art reading column 3, lines 28-30, of Schlichte would take that disclosure to teach that the marker will appear (1) at a later time, and/or (2) at a location *other than* the administration site. For example, Schlichte states that the marker can be given "orally... and appear at a later date or appear in a few hours." Thus, the oral application of the Schlichte marker formulation requires the passage of some amount of time for the marker to appear. Applicants submit that the reason for this time lapse is because, once orally ingested, the marker cannot rapidly appear in cutaneous or subcutaneous tissues since it must first be transported into those tissues.

Such a time lapse is one of the drawbacks discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes.

Further, Schlichte discloses oral application in conjunction with a discussion of other application methods, such as injection. When a substance is injected, it is administered into the venous system, where it is then transported to a different location. Injection, therefore, is not a method used to mark a particular site where the injection itself occurs. Likewise, a marker formulation absorbed orally may then be transported and appear elsewhere. In view of the entire disclosure of Schlichte, Applicants submit that it is clear that this discussion of the marker formulation being injected or given orally only presumes a marker formulation which may then appear at a later time and/or at a location distant to the oral cavity, such as in the cutaneous or subcutaneous tissues of the hide of an animal, which a reading of the entire Schlichte reference will show is the thrust of the disclosure of Schlichte. Again, there is no teaching of a coloration of mucous and/or buccal membranes of the oral and/or pharyngeal cavity.

While column 3 of Schlichte does mention that the marker may appear "in the mouth," again, there is absolutely no disclosure that the marker appears in membranes of the oral and/or pharyngeal cavity, as is recited in claim 15. Applicants assert that a reading of the entire disclosure of Schlichte demonstrates that one skilled

in the relevant art would read that the marker appears in cutaneous or subcutaneous tissues of the mouth. Thus, this disclosure in Schlichte does not teach an oral ingestion of a composition that colors the mucous or buccal membranes of the oral or pharyngeal cavity upon contact therewith.

In view of the above discussion, Applicants respectfully assert that the Schlichte '102 patent does not disclose each and every limitation of claim 15 of the present application and thus, neither does the Schlichte '102 patent disclose each and every limitation of dependent claims 2-14 and 16-27. Applicant thus respectfully requests a withdrawal of the rejection under 35 U.S.C. § 102.

Claim Rejections 35 U.S.C. § 103:

1. **Schlichte**

The Examiner has rejected claims 1-7 and 28 under 35 U.S.C. § 103(a) as being unpatentable over Schlichte. As discussed above, Schlichte has been removed as a reference by filing an affidavit under 37 C.F.R. 1.131, and does not teach or suggest the invention of the present application as presently claimed.

2. **Schlichte/Pather**

The Examiner has rejected claims 8 and 9 under 35 U.S.C. § 103(a) as being unpatentable over the Schlichte '102 patent in view of U.S. Patent No. 6,200,604 (the Pather '604 patent). In particular, the Examiner states that the Pather '604 patent discloses carmine and FD&C dyes, and that it would have been obvious to use such

dyes in the marker composition of the Schlichte '102 patent for oral consumption, as taught by the Pather '604 patent. As discussed above, Schlichte has been removed as a reference by filing an affidavit under 37 C.F.R. 1.131, and does not teach or suggest the invention of the present application as presently claimed. Even considering Schlichte, for the reasons discussed below, Applicants respectfully disagree that the combination of Schlichte and Pather teaches or suggests the presently claimed invention.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses a composition that is directed into cutaneous or subcutaneous tissues of a subject. The disclosure in the Schlichte '102 reference teaches only some time-consuming marking of such cutaneous or subcutaneous tissue, through invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does reference "oral" application or the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for coloration of a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. By contrast, the claims of the present application recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the

cutaneous or subcutaneous tissue as taught by the Schlichte '102 reference. Thus, even if one were to combine the dyes of Pather with the composition of Schlichte, Applicants submit that such a combination would not teach each and every limitation of the claims since the composition would be directed into cutaneous or subcutaneous tissues.

3. Singh/Pather

The Examiner has rejected claim 21 under 35 U.S.C. § 103(a) as being unpatentable over Singh in view of Pather (U.S. Patent No. 6,200,604). The Examiner states that Singh does not teach carmine red but that Pather does teach its use. Applicants respectfully disagree that claim 21 is obvious over Singh in view of Pather.

Claim 21 depends from claim 15 and thus incorporates the limitations of claim 15. As described above, claim 15 is not anticipated by Singh. Thus, for claim 21 to be rendered obvious by the combination of Singh and Pather, claim 15 must either (1) be anticipated by Pather, or (2) be obvious in view of Singh and Pather. However, Applicants assert that neither Singh nor Pather teaches a coloring agent provided in an amount to cause coloration of the oral and/or pharyngeal cavity to determine compliance with a medication regimen. Thus, neither Singh nor Pather, alone or in combination, can anticipate or render obvious claim 15. And thus, the combination of Singh and Pather cannot render claim 21 obvious.

As described above, Applicants assert that there is absolutely no teaching in Singh that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. As described above with respect to the rejection under 35 U.S.C. § 102, the amount of coloring agent in the Singh composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to be visually observable.

Nor does Pather disclose a marker in an amount sufficient to cause contact coloration in an oral and/or pharyngeal membrane to be observed to determine compliance with a medication regimen. Pather is directed to a sublingual buccal effervescent. Applicants note that while Pather does list various coloring agents, including carmine, in an oral composition, such coloring agents find their use solely for the purpose of imparting a particular color to the composition of Pather. They have no purpose and indeed teach no purpose beyond that. In other words, like the coloring agents of Singh, the coloring agents of Pather are used to provide an aesthetic,

cosmetic characteristic (color) to the composition, much like a flavoring agent would be used to make the composition more palatable. There is no teaching in Pather that such coloring agents function as anything but as a superficial component for aesthetic and cosmetic purposes. Again, these are essentially optional components with respect to the therapeutic action provided by the composition. The Pather references does not inherently disclose utilizing a marker in a form and sufficient amount to cause coloration of a patient cavity enabling subsequent visual observation.

Applicants submit that the use of coloring agents as optional components in Pather is very apparent when one considers the disclosure of column 5, lines 1-6 when taken in view of the paragraph at column 4, lines 52-58 of Pather. The paragraph concerning coloring at column 5, lines 1-6 is introduced earlier in the paragraph of column 4, lines 52-58 as a mere list of ingredients which may be included in the composition. These ingredients may include "glidants, lubricants, binders, sweetener, flavoring, and coloring components." The subsequent paragraphs go on to simply list examples of these coloring ingredients. However, there is no indication that the coloring agent plays any significant role in the composition of Pather, nor does Pather teach that the coloring agent is present in a form and amount sufficient to stain the oral and/or pharyngeal cavity for subsequent visual observation to determine compliance with a medication regimen. In contrast, the coloring agent of the composition of the present application is what allows an observer to determine compliance, duration since

last medication, remaining time until next medication, etc. There simply is no teaching in Pather by which one of skill in the art may use the composition disclosed therein to obtain such information.

Further, as mentioned above, Applicants assert that there is absolutely no teaching in Pather that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. First, the composition of Pather is taught as having a wholly different purpose than that of the present application. Reference to the entirety of Pather makes it quite clear that the purpose of the composition of that reference lies in that it includes an effervescent to promote absorption of the medicament directly into the oral cavity. Nowhere does Pather discuss or teach that the use of the coloring agent is part of a method for monitoring patient compliance. Rather, as described above, the coloring agent of Pather is merely used to impart an aesthetic, cosmetic quality to the composition. Second, the amount of coloring agent in the prior art composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Pather, the amount of coloring agent in the composition is recited at column 5 as 0.1 - 3.5 weight percent of the total composition.

Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the prior art composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. Like Singh, as may be appreciated, this defeats the entire purpose of the invention.

Further, claim 15 has been presently amended to recite that the half-life of the marker is comparable to the half-life of the composition. Support for this amendment may be found at least in originally filed claim 20. Applicants submit that the half-life of the colorant in Singh (based on the amounts disclosed) would not be similar to, and thus comparable to, the half-life of the composition. This, again, is because the colorant of Singh is only present in a small amount to be used as an optional component. Likewise, the half-life of the colorant in Pather would not be similar to, and thus comparable to, the half-life of the composition.

Therefore, neither Singh nor Pather discloses a marker provided in a sufficient amount and form to cause a contact coloration of at least a portion of the oral and/or pharyngeal cavity for determining whether a patient is in compliance with a medication regimen. Thus, any combination of Singh and Pather does not disclose this limitation of claim 15, which is incorporated in claim 21. As a result, claim 21 cannot be rendered obvious by the combination of Singh and Pather. Further, since Singh and

Pather (and the colorants thereof) are directed to different compounds with different uses for different purposes, there would be no motivation for one skilled in the art to combine the two references. Applicants thus respectfully request a withdrawal of the rejection of claim 21.

4. **Singh/Blase**

The Examiner has rejected claims 23 and 25-27 under 35 U.S.C. § 103(a) as unpatentable over Singh in view of U.S. Patent No. 5,272,137 (Blase). In particular, the Examiner states that Singh does not disclose multiple markers, but that these are disclosed by Blase. Applicants respectfully disagree.

Claims 23 and 25-27 each ultimately depend from claim 15 and thus incorporate the limitations of claim 15. As described above, claim 15 is not anticipated by Singh. Thus, for claims 23 and 25-27 to be rendered obvious by the combination of Singh and Blase, claim 15 must either (1) be anticipated by Blase, or (2) be obvious in view of Singh and Blase. However, Applicants assert that neither Singh nor Blase teaches a coloring agent provided in an amount to cause coloration of the oral and/or pharyngeal cavity to determine compliance with a medication regimen. Thus, neither Singh nor Blase, alone or in combination, can anticipate or render obvious claim 15. And thus, the combination of Singh and Blase cannot render claims 23 and 25-27 obvious.

As described above, Applicants assert that there is absolutely no teaching in Singh that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. In particular, the amount of coloring agent in the prior art composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to be visually observable.

Applicants further submit that Blase does not cure the defects of Singh, because Blase does not provide any of the elements of claim 15 that are missing from Singh. Blase does not teach contact coloration to be observed to determine compliance. In Blase, the amount of coloring agent in the composition is recited in Table 1 and in the Example as between .0005 and .003 g per 100 ml of the composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient.

Further, claim 15 has been presently amended to recite that the half-life of the marker is comparable to the half-life of the composition. Support for this

amendment may be found at least in originally filed claim 20. Applicants submit that the half-life of the colorant in Singh (based on the amounts disclosed) would not be similar to, and thus comparable to, the half-life of the composition. This, again, is because the colorant of Singh is only present in a small amount to be used as an optional component. Likewise, the half-life of the colorant in Blase would not be similar to, and thus comparable to, the half-life of the composition.

Also, the Examiner cites Blase for its disclosure of multiple dyes (being multiple markers). Applicants disagree. The purpose of using multiple dyes in one composition in Blase is to mix two colors to produce a third color for the suspension (see column 10, lines 6-9, discussing the mixing of blue and red coloring agents to provide a purple color to the composition). This in no way discloses multiple markers as described in the present application (for example, see p. 17, lines 6-16 of the application, disclosing a composition including a first marker detectable under natural light and a second marker detectable only under light that causes fluorescence, wherein each marker has a different duration).

Thus, neither Singh nor Blase discloses a marker provided in a sufficient amount and form to cause a contact coloration of at least a portion of the oral and/or pharyngeal cavity for determining whether a patient is in compliance with a medication regimen. Thus, any combination of Singh and Blase does not disclose this limitation of claim 15, which is incorporated in claims 23 and 25-27. Thus, claims 23 and 25-27

Schlichte '102 patent only discloses a composition that is directed into cutaneous or subcutaneous tissues of a subject. The disclosure in the Schlichte '102 reference teaches only some time-consuming marking of such cutaneous or subcutaneous tissue, through invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does reference "oral" application or the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for coloration of a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. By contrast, the claims of the present application recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the cutaneous or subcutaneous tissue as taught by the Schlichte '102 reference. Thus, even if one were to combine the dyes of Pather with the composition of Schlichte, Applicants submit that such a combination would not teach each and every limitation of the claims since the composition would be directed into cutaneous or subcutaneous tissues.

6. Schlichte/Kell

The Examiner has rejected claims 12-14, 23, and 25 under 35 U.S.C. § 103(a) as being unpatentable over the Schlichte '102 patent in view of U.S. Patent No. 5,776,783 (the Kell '783 patent). In particular, the Examiner states that the

Schlichte '102 patent discloses a composition having multiple medications, but does not disclose a marker associated with each medicament. The Examiner then asserts that the Kell '783 patent teaches a composition having multiple medications and separate markers associated with each medication in the formulation to monitor compliance with drug ingestion. The Examiner states that it therefore would have been obvious to provide multiple medications with markers associated with each medication in the composition of the Schlichte '102 patent wherein each marker has a unique coloring characteristic and residence time in the tissue to monitor compliance with drug ingestion, as taught by the Kell '783 patent. The Examiner finally asserts that the marker may be any color and is visible under a variety of lighting conditions, as taught by the Schlichte '102 patent. As discussed above, Schlichte has been removed as a reference by filing an affidavit under 37 C.F.R. 1.131, and does not teach or suggest the invention of the present application as presently claimed. Even considering Schlichte, for the reasons discussed below, Applicants respectfully disagree that the combination of Schlichte and Kell teaches or suggests the presently claimed invention.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses a composition that is directed into cutaneous and subcutaneous tissues of a subject. The disclosure in the Schlichte '102 reference teaches only some marking of such cutaneous or subcutaneous tissue, through

invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does minimally refer to "oral" application and the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for coloring a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. By contrast, the newly added claims recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. As above, Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the cutaneous or subcutaneous tissue as taught by the Schlichte '102 reference. Thus, even if one were to combine the multiple markers of Kell with the composition of Schlichte, Applicants submit that such a combination would not teach each and every limitation of the claims, since the composition would be directed into cutaneous and subcutaneous tissues.

Further, Applicants assert that, were one to combine the Schlichte '102 patent and the Kell '783 patent, the combination does not teach the invention because the Kell '783 patent discloses a method of monitoring patient compliance with a medical regimen by testing the urine of a patient. Thus, Kell also does not teach the contact coloration of a mucous or buccal membrane. Additionally, analysis of urine is a process that is time consuming, intrusive, requires scheduling, and requires the presence of a trained technician. These are the very drawbacks of current monitoring methods, described in the "Background of the Invention" section of the present application, that

the present invention eliminates. In fact, urine analysis was one of the prior art monitoring methods that was discussed in the present application as wholly different than the compliance monitoring composition and method of the present invention. Even if one skilled in the art were to combine the teachings of Schlichte and Kell, they would not be directed to oral ingestion of a composition for contact coloration of a mucous or buccal membrane.

The present invention, by contrast, is rapid, simple, non-invasive, and inexpensive in that it is simply performed by observing a mucous or buccal membrane of the oral/pharyngeal cavity after oral ingestion for staining in order to determine compliance. Applicants thus respectfully assert that even if one were to attempt to detect the coloring agent of the Schlichte '102 patent, it could not be detected in the urine by the method disclosed by the Kell '783 patent, since such coloring agent would not be detectable in a patient's urine. Nor would such a coloring agent be visually observable in a patient's urine.

Conclusion:

For the foregoing reasons, Applicants submit that all claims are patentable and a Notice of Allowance is respectfully requested.

The Commissioner is hereby authorized to charge Deposit Account No. 23-3000 in the amount of $60.00 for a one-month extension of time. No additional fee is believed due with this submission. However, if any additional fee or surcharges are

deemed due, please charge same or credit any overpayment to Deposit Account No. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,

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